XVI. Tumours of the female genital tract

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Tumours of the female tubular genital tract are comparatively rare, with the exception of leiomyomas in cows and bitches, uterine carcinomas and vaginal fibropapillomas in cows, and transmissible venereal tumours in bitches. Uterine adenocarcinomas of cows are highly scirrhous, often causing minimal gross lesions that remain undetected until metastatic lesions in pelvic nodes and lungs are found. Cats and bitches also develop uterine carcinomas, but less frequently than cows; when present, they are predominantly discrete masses of well differentiated, non-sclerosing adenocarcinoma. Fibropapillomas are caused by the virus of verrucca vulgaris and can be transmitted to the penis of the bull. Adenomyosis is not uncommon in the cat, cow, and bitch. There is a marked difference in the frequency with which cervical carcinomas occur in man compared with other mammals; in the latter we could find no instance of an unequivocal primary cervical carcinoma. There are a few reports describing invasive carcinomas involving the cervix, but invasion from either a uterine or a vaginal carcinoma could not be ruled out.

This classification deals with tumours of the female tubular genital tract, excluding the ovary and the cutaneous part of the vulva. The ovary is dealt with separately [a] because of its great variety of tumours, and tumours of the vulvar skin comprise the same types that occur in other areas of hair-bearing skin described elsewhere.[b]

Tumours of the female tubular genital tract are comparatively rare in domestic animals, with the exception of leiomyomas in cows and bitches, vulvovaginal fibropapillomas in cows, and transmissible venereal tumours in bitches. There is a marked difference between humans and domestic animals in the frequency with which cervical carcinomas occur; no unequivocal case of primary cervical carcinoma was found in domestic animals. There are a few reports describing invasive carcinomas involving the cervix, but invasion from either a uterine or vaginal carcinoma could not be ruled out.

The classification is based on material collected at New York State College of Veterinary Medicine and the University of Connecticut, and on additional material generously made available by: Mr K. Head, University of Edinburgh; Dr E. Weiss, University of Giessen; Dr J. Mouwen, University of Utrecht; Dr B. Schieffer, University of Saskatchewan; Dr C. Appleby, Royal Veterinary College, London; Dr A. L. Parodi, Alfort, France; and Dr V. E. Osborne, University of Sydney.

HISTOLOGICAL CLASSIFICATION AND NOMENCLATURE OF TUMOURS OF THE FEMALE GENITAL TRACT

I. TUMOURS OF THE UTERINE TUBE

A. EPITHELIAL TUMOURS
1. Adenoma
2. Adenocarcinoma

B. MESENCHYMAL TUMOURS
1. Lipoma

C. TUMOUR-LIKE LESIONS

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[a] See page 203 of this issue.

[b] WEISS, E. & FRESE, K. *Bulletin of the World Health Organization*, **50**: 79-100 (1974); and WEISS, E. *Bulletin of the World Health Organization*, **50**: 101-110 (1974).

II. TUMOURS OF THE UTERUS

A. EPITHELIAL TUMOURS
1. Adenoma
2. Adenocarcinoma

B. MESENCHYMAL TUMOURS
1. Fibroma
2. Fibrosarcoma
3. Leiomyoma
4. Leiomyosarcoma
5. Lipoma
6. Lymphosarcoma

C. UNCLASSIFIED TUMOURS

D. TUMOUR-LIKE LESIONS
1. Adenomyosis
2. Cystic endometrial hyperplasia
3. Endometrial polyp
4. Lymphangiectasia
5. Mesonephric duct cysts
6. Serosal cysts
7. Subinvolution of placental sites
8. Squamous metaplasia

III. TUMOURS OF THE CERVIX

A. FIBROMA

B. LEIOMYOMA

C. SARCOMAS

D. UNCLASSIFIED TUMOURS

E. TUMOUR-LIKE LESIONS
1. Epithelial inclusion cysts
2. Fibrosis
3. Squamous metaplasia

IV. TUMOURS OF THE VAGINA AND VULVA

A. EPITHELIAL TUMOURS
1. Papilloma
2. Squamous cell carcinoma

B. FIBROPAPILLOMA (FIBROMA)

C. LEIOMYOMA

D. TRANSMISSIBLE VENEREAL TUMOUR

E. LYMPHOSARCOMA

F. FIBROSARCOMA

G. VASCULAR TUMOURS

H. MALIGNANT MELANOMA

I. UNCLASSIFIED TUMOURS

J. TUMOUR-LIKE LESIONS
1. Cysts of Gartner's ducts
2. Cysts of Bartholin's glands
3. Granular vaginitis
4. Herniated adipose tissue
5. Oestrual oedema of the vulva

DESCRIPTION OF TUMOURS

I. TUMOURS OF THE UTERINE TUBE

Tumours of the uterine tube (oviduct) are extremely rare in all species of domestic animal except poultry. Only three cases were available for study in the bitch and one in the mare. None were found in the cat, ewe, sow, or cow.

A. *Epithelial tumours*

1. *Adenoma.* Two tumours appearing as cauliflower-like masses adjacent to the ovary were studied in the bitch. Histologically, they consisted of papillary formations with apparently rather mature epithelium (Fig. 1). In other areas, there was a moderate amount of fibrous tissue and smooth muscle elements (Fig. 2). A more definitive classification should await the study of additional cases.

A single case was studied in the mare. On macroscopic examination, a large papillary mass of tissue was seen to be attached to the fimbriated portion of the uterine tube. Histologically, it closely resembled normal oviduct.

2. *Adenocarcinoma.* One epithelial tumour of the canine uterine tube had spread to the peritoneal cavity by implantation. On histological examination,

it closely resembled the canine adenomas described above.

B. *Mesenchymal tumours*

1. *Lipoma.* This is a rare tumour of the ovarian bursa of the bitch. It is made up of abundant, apparently mature adipose tissue.

C. *Tumour-like lesions*

Paramesonephric (müllerian) duct cysts, attached to the fimbriated portion of the uterine tube, occur frequently in all species of domestic animal. They are blind, accessory oviducts and, in the larger species, may become several centimetres in diameter. The so-called hydatid of Morgagni is a large, cystic, accessory oviduct.

II. TUMOURS OF THE UTERUS

A. *Epithelial tumours*

1. *Adenoma* (Fig. 3). This is a rare tumour consisting of a discrete nodule of well differentiated endometrial glandular tissue. It has varying amounts of fibrous stroma and may resemble adenomyoma. It may form a polypoid protrusion into the uterine lumen.

2. *Adenocarcinoma* (Fig. 4–8). This tumour is rare in all species of domestic animal except cows and rabbits. In cows, it represents one of the three most common neoplasms encountered, following lymphoma and eye cancer. It occurs in old cows (usually over six years of age) and often as a silent lesion that is not detected clinically unless large metastases are present in the nodes and lungs. During meat inspection, only minimal macroscopic changes are seen in the uterus; there is diffuse enlargement of the wall, which on cutting may reveal hard white nodules. Histologically, the bovine form is a scirrhous adenocarcinoma that diffusely invades all layers of the wall; scattered clusters of tumour cells may be seen throughout the myometrium, sometimes within vascular spaces and often between muscle bundles. Marked fibrosis accompanies the invasion. The rate of metastasis to the internal iliac nodes and lungs is very high.

In bitches and cats, the tumour is a non-sclerosing adenocarcinoma that typically produces a distinct mass with distortion of the mucosa. The tumour usually comprises well differentiated, glandular structures with distinct lumen formation, lined by tall cylindrical cells.

B. *Mesenchymal tumours*

1. *Fibroma.* Fibromas are benign, hard, white, spherical tumours of the uterine wall and occasionally occur in bitches and cows. They may be single or multiple and consist of dense masses of collagenous fibrous tissue.

2. *Fibrosarcoma.* This is a very rare tumour in most species of animal and only a few cases have been recorded in cows, mares, and bitches. It has the same morphological features as fibrosarcoma of the soft (mesenchymal) tissues described previously.[a]

3. *Leiomyoma* (Fig. 9). Leiomyomas are benign, firm, tan-coloured, nodular tumours of the myometrium and most frequently occur in the cow, cat, and bitch. The tumour is made up of bundles of intertwining smooth muscle cells, frequently interspersed with collagen fibres. Central necrosis occurs in many of the larger neoplasms.

4. *Leiomyosarcoma* (Fig. 10). Leiomyosarcomas are rare but have been recorded in the cat, cow, bitch, and mare. The tumours are similar to leiomyomas but are more cellular and have larger, hyperchromatic nuclei and moderate numbers of mitotic figures.

5. *Lipoma.* This is a rare tumour that occurs in the broad ligament of the canine uterus and is composed of mature adipose cells. No liposarcomas have been found.

6. *Lymphosarcoma.* This tumour occurs quite frequently in cows but rarely in bitches, sows, mares, and cats. It has the same morphological features as lymphosarcoma of the haematopoietic and lymphoid tissues described previously.[b]

C. *Unclassified tumours*

These are tumours that cannot be placed in any of the above categories.

D. *Tumour-like lesions*

1. *Adenomyosis* (Fig. 11). Adenomyosis of the uterus refers to the presence of endometrium within the myometrium. Endometrial glands with a supporting stroma are often adjacent to large blood vessels. The condition should not be confused with

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[a] WEISS, E. *Bulletin of the World Health Organization*, **50**: 101-110 (1974).

[b] JARRETT, W. F. & MACKEY, L. J. *Bulletin of the World Health Organization*, **50**: 21-34 (1974).

endometriosis, which is a disease of primates only (including some species of laboratory monkey). The use of the term " internal endometriosis " for adenomyosis often leads to confusion. Adenomyosis occurs in all species of domestic animal but most frequently in the cat, cow, and bitch.

2. *Cystic endometrial hyperplasia* (Fig. 12–14). This may result from either estrogenic or progestational stimulation, depending on the species involved. In ewes and cows, cystic hyperplasia of the endometrium is associated with prolonged estrogenic stimulation, either from the ovary, from injected estrogen, or from ingested subterranean clover.

In the bitch, there are three morphologically distinct types of endometrial hyperplasia: " cystic hyperplasia–pyometra complex " due principally to progesterone; cystic hyperplasia due to certain estrogenic compounds; and pseudopregnancy. In the cat, " cystic hyperplasia–pyometra complex " is also due to progesterone.

The cause of cystic hyperplasia of the endometrium has not been established in the sow and mare.

3. *Endometrial polyp.* Endometrial polyps are focal proliferations of glandular and stromal elements of the endometrium that occur in the bitch and cat. The stroma is usually oedematous.

4. *Lymphangiectasia.* Widely dilated lymphatics occur in the ventral part of the body of the uterus in aged mares.

5. *Mesonephric duct cysts.* Remnants of the mesonephric duct persist in the mesometrium and myometrium of all species of domestic animal, and large cystic remnants have been found in the bitch and cow. The epithelium is usually cuboidal with clear cytoplasm. There are two muscular coats surrounding the epithelium-lined canal.

6. *Serosal cysts.* Cysts lined with peritoneum occur in the uterine serosa of mature and aged cows and bitches that have undergone previous pregnancies. In the bitch they are most prominent on the antimesometrial side of the uterus and in the cow on the intercornual ligament.

7. *Subinvolution of placental sites* (Fig. 15). This condition occurs in bitches, the majority of which are under three years of age. Persistent discharge of blood follows whelping. Macroscopic examination of the uterus reveals enlargements at the sites of placental attachment. Large cells with abundant eosinophilic cytoplasm are present in the stroma in the areas of uterine enlargement, and these groups of cells may be surrounded by lymphocytes, plasma cells, and haemosiderin-laden macrophages. The large eosinophilic cells sometimes invade the myometrium. The origin of the large cells has not been established but they may be of trophoblastic derivation.

8. *Squamous metaplasia* (Fig. 16). Squamous metaplasia of the surface endometrium occurs in some cases of pyometra in all species. It occurs in ewes poisoned by highly chlorinated naphthalenes. The entire endometrium may be transformed into squamous tissue.

III. TUMOURS OF THE CERVIX

A. *Fibroma*

This is similar to fibroma of the uterus (see p. 219).

B. *Leiomyoma*

This is similar to leiomyoma of the uterus (see p. 219).

C. *Sarcomas*

Fibrosarcoma, leiomyosarcoma, and lymphosarcoma occasionally involve the cervix.

D. *Unclassified tumours*

These are tumours that cannot be placed in any of the above categories.

E. *Tumour-like lesions*

1. *Epithelial inclusion cysts.* These follow injury, which results in the development of epithelial cysts lined with cuboidal-to-flattened cervical epithelium.

2. *Fibrosis.* Fibrosis of the cervix develops in cows and ewes following repeated pregnancies. The cervical rugae, especially those near the vagina, become traumatized during parturition and there is a diffuse proliferation of fibrous tissue. The enlarged rugae then protrude into the vagina.

3. *Squamous metaplasia.* Squamous metaplasia may develop following prolonged estrogenic stimulation. It also develops in the tips of fibrotic cervical rugae that have prolapsed.

IV. TUMOURS OF THE VAGINA AND VULVA

The tumours of the vagina and of the mucous membrane portion of the vulva are similar in

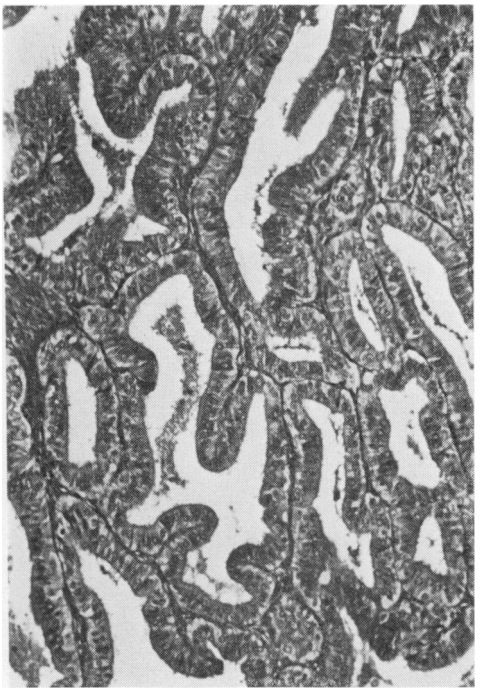

Fig. 1. Adenoma of the uterine tube (oviduct) (bitch).

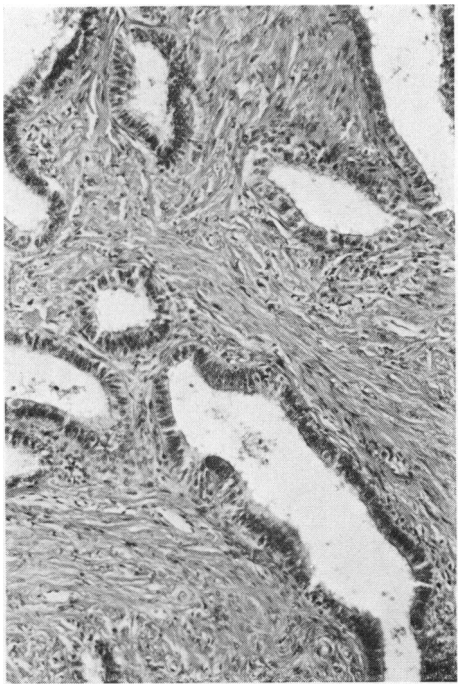

Fig. 2. Adenoma of the uterine tube with fibromuscular component (bitch).

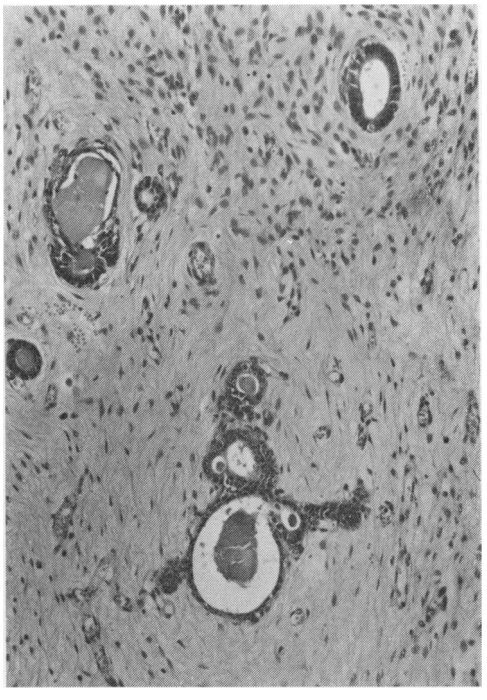

Fig. 3. Adenoma of the uterus with abundant fibrous stroma (bitch).

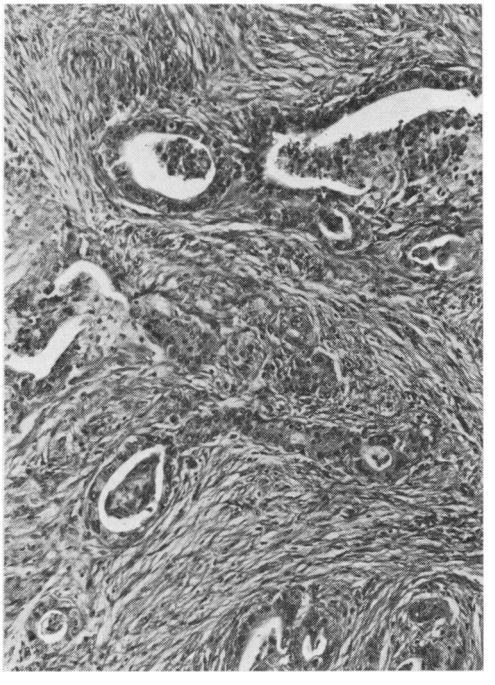

Fig. 4. Adenocarcinoma of the uterus (cow).

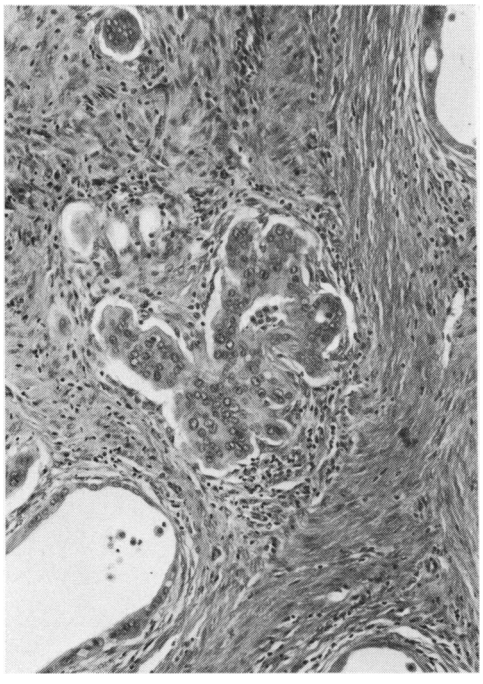

Fig. 5. Adenocárcinoma of the uterus (cow).

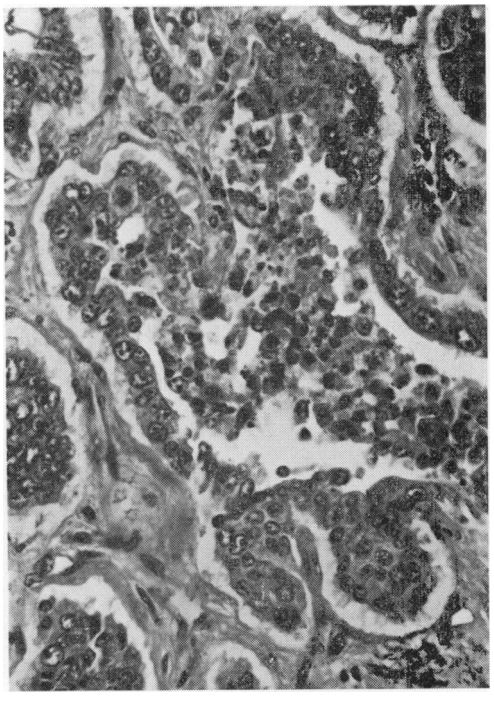

Fig. 6. Uterine adenocarcinoma, metastasis in lung (cow).

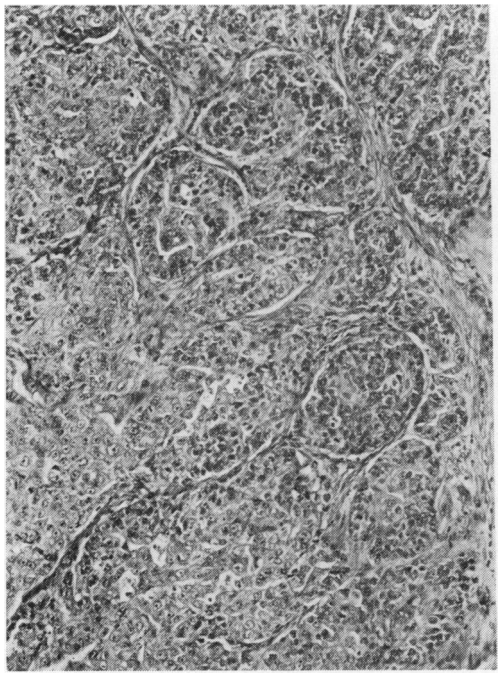

Fig. 7. Adenocarcinoma of the uterus (bitch).

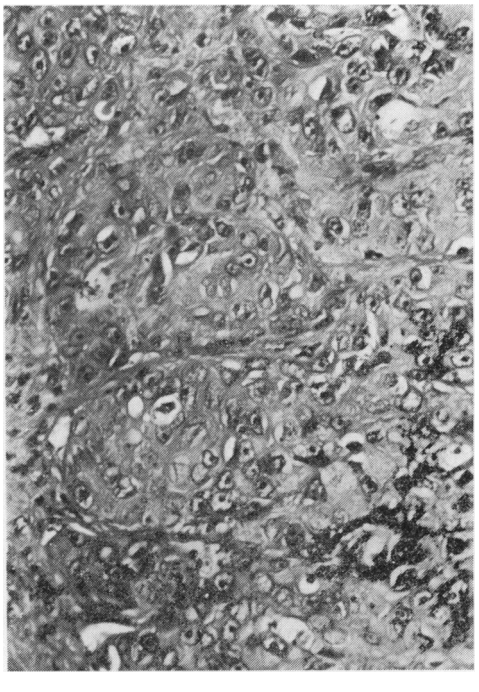

Fig. 8. Adenocarcinoma of the uterus (bitch).

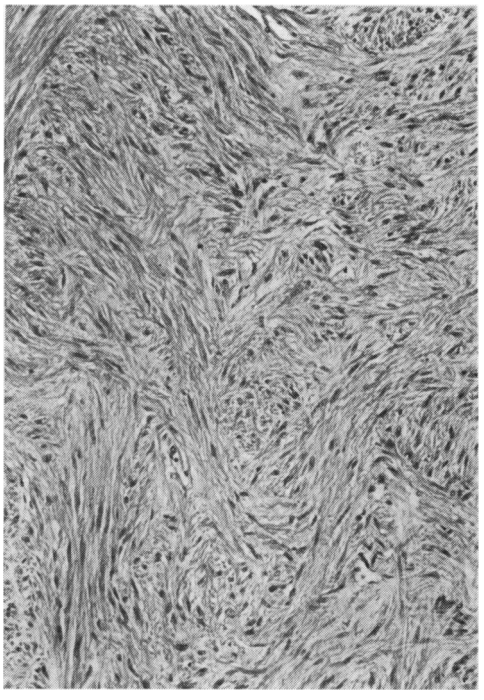

Fig. 9. Leiomyoma of the uterus (sow).

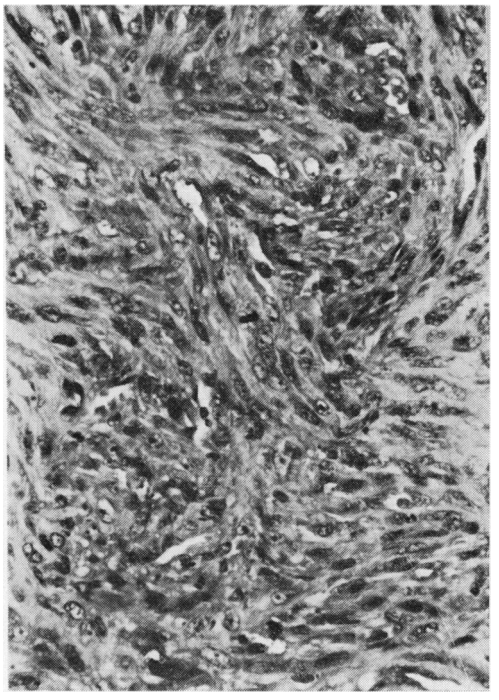

Fig. 10. Leiomyosarcoma of the uterus (cat).

Fig. 11. Adenomyosis of the uterus (cow).

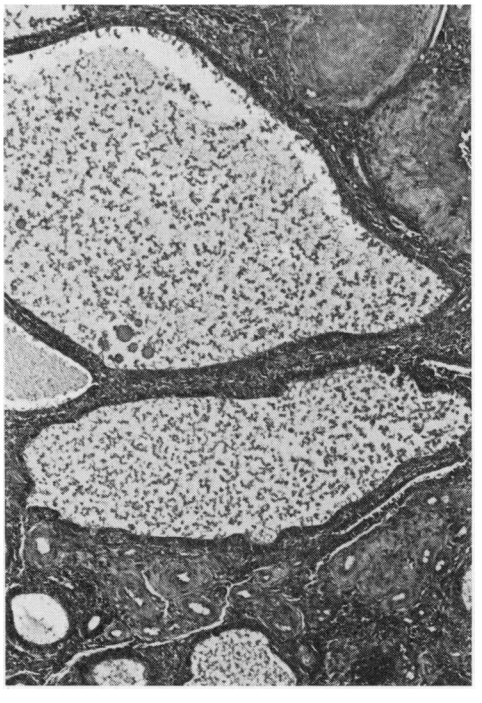

Fig. 12. Cystic uterine hyperplasia associated with cystic ovaries (cow).

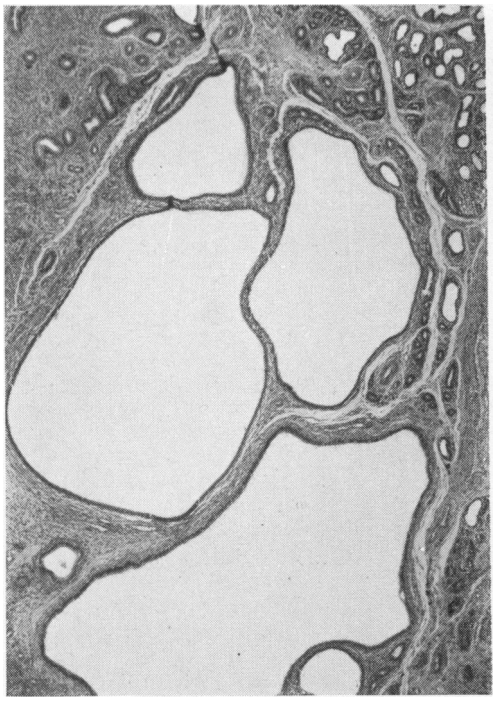

Fig. 13. Cystic uterine hyperplasia caused by subterranean clover (ewe).

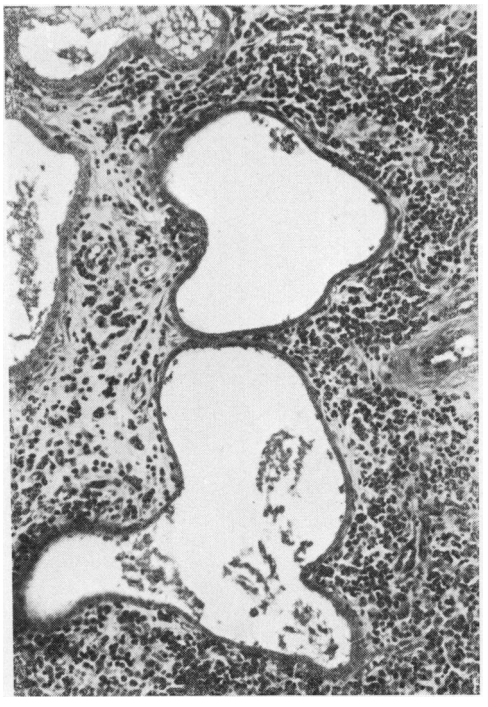

Fig. 14. Cystic uterine hyperplasia of pyometra (bitch).

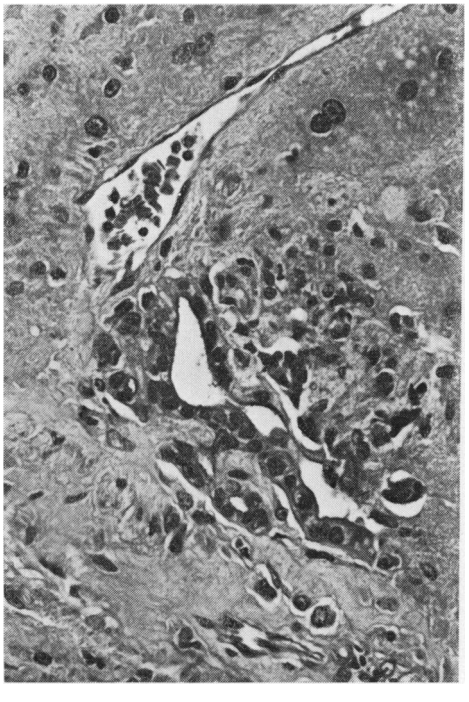

Fig. 15. Uterine subinvolution site (bitch).

Fig. 16. Uterine squamous metaplasia caused by chlorinated naphthalene (ewe).

morphological appearance to those of the penis and uterus. The reader is referred to the illustrations accompanying the classification of tumours of these two sites.[a]

A. *Epithelial tumours*

1. *Papilloma.* This is a rare, benign, epithelial, keratinizing, papilliform tumour with scant fibrous stroma; it is usually small, but may occasionally reach a large size. Lymphoplasmacytic infiltration is frequent at the base of the tumour. A virus-induced papilloma, which is venereally transmitted, occurs in the pig.

2. *Squamous cell carcinoma.* This is the malignant counterpart of squamous papilloma and is made up of large epithelial cells showing intercellular bridges and keratin formation; keratin occurs either as pearls or, in less well differentiated carcinomas, as keratinized single cells. It occurs most frequently in the cow, mare, and bitch. Most tumours occur as cauliflower-like masses on or near the vulvar skin junction. The tumour has great propensity for invasion and for metastasis to the superficial and deep inguinal lymph nodes and lungs. If only a limited amount of biopsy material is available, it may be extremely difficult to differentiate between squamous papillomas and squamous cell carcinomas.

B. *Fibropapilloma (fibroma)*

This is a benign tumour, which is composed mainly of fibroblasts but is also associated with marked epithelial proliferation, not only on the surface but extending deeply into the fibromatous centre; this is similar to the pseudoepitheliomatous hyperplasia seen in some forms of epulis. The fibroblasts are arranged in intertwining fascicles with different amounts of collagen. If only a limited amount of biopsy material is available, it may be difficult to differentiate fibrosarcomas from rapidly growing fibropapillomas. The tumour is often fungoid and may be attached either by a broad base or by a long pedicle that allows some of the tumour to protrude from the vulva. The tumours are usually small, measuring less than 3 cm across, but they may reach a large size. Their presence may seriously interfere with copulation because of pain or mechanical interference. Ulceration and haemorrhage are frequent, particularly with large tumours. Spontaneous regression frequently occurs.

Fibropapillomas can be transmitted experimentally with cell-free material to the penile or vaginal mucosa. The causative virus appears to be that which also causes cutaneous warts (verruca vulgaris) in cattle. Young calves are easier to infect than older cattle, indicating that immunity may be acquired.

C. *Leiomyoma*

Leiomyomas are benign, firm, white, nodular tumours of the vaginal wall and occur most frequently in bitches. The tumour is made up of bundles of intertwining smooth muscle cells, frequently interspersed with collagen fibres. These tumours appear identical to uterine leiomyomas.

D. *Transmissible venereal tumour*

This neoplasm is composed of tumour cells forming diffuse masses or sheets beneath the mucosa. The tumour cells usually extend up to the stratum germinativum of the mucosa. The surface epithelium is frequently hyperplastic and occasionally ulcerated. Fibrous connective tissue trabeculae containing blood vessels traverse the neoplastic masses in an irregular fashion and provide a supporting framework for the tumour. The blood vessels are frequently congested. For the most part, the tumour cells are in close apposition to one another so that cell borders are difficult to discern. In areas where the cell population is less dense, distinct ovoid or round cytoplasmic outlines can be seen. The neoplastic cells have abundant, darkly eosinophilic cytoplasm with a finely reticulated, often foamy appearance, and large round-to-oval or, rarely, U-shaped nuclei. The chromatin is finely stippled and one prominent nucleolus is usually visible in each nucleus. In general, mitoses occur frequently. Lymphocytes and plasma cells are seen in some neoplasms but are absent from others; a few eosinophils are observed in some neoplasms. Infrequently, metastases may occur in regional nodes and these appear similar to the primary tumour. Spontaneous regression is frequent and usually occurs within 2 months.

This tumour, first described 150 years ago in Europe, now has worldwide distribution with enzootic areas in Central America and South-East Asia; in the northern United States, Canada, and northern Europe, however, few bitches are affected. The tumour is transmitted as intact cells by licking, by coitus, or by experimental injection. The modal number of chromosomes in the tumour

[a] For a classification of tumours of the penis see this issue, p. 247.

cells is less than that of normal canine cells (59 as against 78).

E. *Lymphosarcoma*

This tumour occurs frequently in cows and rarely in bitches, sows, and cats. It has the same morphological features as lymphosarcomas of the haematopoietic and lymphoid tissues.[a]

F. *Fibrosarcoma*

This is a rare tumour in most species of domestic animal and only a few cases have been recorded in cows, mares, and bitches. It has the same morphological features as fibrosarcoma of the soft (mesenchymal) tissues.[b]

G. *Vascular tumours*

Haemangiomas and haemangiosarcomas are rare and of the same morphological appearance as those of the soft (mesenchymal) tissues.[b]

H. *Malignant melanoma*

This is a tumour, encountered particularly in old grey mares, in which large nodular and ulcerating masses of melanomas are present in the vulva and perineum. For a histological classification see that of the tumours of the skin.[c]

I. *Unclassified tumours*

These are tumours that cannot be placed in any of the above categories.

J. *Tumour-like lesions*

1. *Cysts of Gartner's ducts.* Portions of the mesonephric ducts in the vagina are commonly referred to as Gartner's ducts. Cystic Gartner's ducts are very rare in virgin females but are seen quite frequently in animals that have given birth repeatedly and have had the opportunity to develop vaginal infections. In cases of naphthalene poisoning Gartner's ducts undergo squamous metaplasia and cyst formation.

2. *Cysts of Bartholin's glands.* These glands in the lateral walls of the vagina may become cystic owing to occlusion of the ducts. This may occur after inflammatory or metaplastic processes, and may be associated with cystic ovaries in cows.

3. *Granular vaginitis.* Granular vaginitis is a common disease of cows in which lymphoid follicles are found in the submucosa, causing nodular white elevation of the vaginal and vulvar mucosa.

4. *Herniated adipose tissue.* During parturition in excessively fat cows, the junction of the vulva and vagina may become lacerated, allowing a mass of perineal adipose tissue to protrude into the lumen of the genital tract. The surface of the protruding adipose tissue becomes covered by granulation tissue.

5. *Oestrual oedema of the vulva.* A large focal area of oedema of the vulva sometimes develops during estrus in the bitch and the oedematous mass of tissue frequently protrudes from the vulva. Although this condition has been referred to as hyperplasia and hypertrophy of the vulva, the predominant lesion is oedema of the subepithelial connective tissue. Fibrosis develops in chronic cases.

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[a] JARRETT, W. F. & MACKEY, L. J. *Bulletin of the World Health Organization*, **50**: 21-34 (1974).

[b] WEISS, E. *Bulletin of the World Health Organization*, **50**: 101-110 (1974).

[c] WEISS, E. & FRESE, K. *Bulletin of the World Health Organization*, **50**: 79-100 (1974).